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Epidural Fentanyl Vs Epidural Clonidine for Postoperative Analgesia: A Comparative Study.

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ABSTRACT

Background: Various research studies are undergoing to find out better adjuvants to local anaesthetics for prolongation of post-operative analgesia. Fentanyl is most commonly used adjuvant for post-operatve analgesia. Clonidine, an α2-agonist also used as an adjuvant to local anaesthetics. The aim of our study was to compare the block characteristics & other side effects between epidural fentanyl and epidural clonidine as an adjuvant to bupivacaine. **Methods**: After taking approval from hospital ethical committe , a prospective randomised double blind study was carried out taking 90 adult patients of ASA Grade I & II between age 18 -60 years of either sex and randomly allocated into 3 equal groups. Group I – Control group – Bupivacaine alone, Group II – Epidural bupivacaine with clonidine, Group III – Epidural bupivacaine with fentany[1] **Results:** Group II & III had rapid onset of action than Group I . Onset & duration of motor block was comparable in all the three groups. Two segment regression time was prolonged in Group II & Group III than Group I. Duration of analgesia was prolonged in Group II in comparison to Group III & Group I which is statistically significant. Hemodynamic parameters were comparable between all the groups. Side effects were minimal. **Conclusion**: Adjuvants added to bupivacaine always better than plane bupivacaine for neuraxial block. Epidural clonidine with bupivacaine is a better alternative to epidural fentanyl bupivacaine combination.

Keywords: Clonidine, Epidural Anaesthesia, Fentanyl, Post-Operative Analgesia.

INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or in terms of such damage. Post-surgical pain is a complex response to tissue trauma during surgery. Post-operative pain increases the possibility of post-surgical complication, interferes with recovery and return to normal activities. Adequate post-operative pain relief reduces the incidence of pulmonary complications like hypoxia, hypercarpia, retention of secretion, atelectasis and pneumonia and it allows early ambulation.

Intrathecal use of narcotics like fentanyl, tramadol etc and non-narcotics like clonidine provides a limited duration of post-operative pain relief. Epidural administration of analgesics raise new hope for post-operative analgesia. Pages[1] 1st used lumbar epidural analgesia for surgery and Behar et al[2] used epidural morphine for pain relief. Clonidine is α2adenoreceptor agonist prolonged duration of analgesia intrathecally or in epidural space.[1,2] Fentanyl a μ-opioid receptor agonist used effectively as an alternative to morphine.

The aim of this study is to compare the effect of epidural clonidine and epidural fentanyl as an adjuvant to epidural bupivacaine hydrochloride for post-operative analgesia.

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MATERIALS AND METHODS

A prospective randomized double blind controlled study was carried out on 90 patients of both sex aged between 18-60 years of ASA I and II for lower abdominal surgical procedures. Ethical committee approval taken prior to study. Pre- aneathetic check-up evaluated including routine pre-operative investigation. A well informed written consent was taken. Normal neuraxial exclusion criteria were followed. 90 patients were randomly distributed into three equal groups.

GpI (n=30)-0.5% bupivacaine Hcl (20 ml) +normal saline (2 ml) [control]

GpII (n=30)-0.5% bupivacaine Hcl (20 ml) +clonidine 100μg (0.66ml) +normal saline (1.34ml)

GpIII (n=30)-0.5% bupivacaine Hcl(20ml)+fentanyl 100μg(2ml)

Patients were kept nil orally 6-8 hrs prior to surgery and tab alprazolam 0.5mg, tab ranitidine 300mg given night before surgery. After taking proper aseptic measures L3-L4 lumbar interspace infiltrated with1% lignocaine hydrochloride 2ml using 26 guage hypodermic needle. Epidural space identified with Tuohy needle 16 guage with LOR technique. Epidural catheter placed 5cm in the epidural space. Epidural Test dose found negative. Patients were monitored for haemodynamics,respiratory rate (RR) at 0, 5, 10, 20, 30, 45, 60, 90 minutes;2, 4, 8hrs intervals from completion of epidural drug administration.

Following parameters were observed

1. Onset of sensory blockade i.e. time from epidural injection till loss of sensation at T10 dermatome.
2. Highest level of sensory block.
3. Time taken to achieve highest level of sensory block.
4. Time taken for onset of motor blockade i.e. from end of epidural injection till Grade III motor blockade. (bromage)
5. Two segment sensory regression.
6. Duration of motor block i.e. onset of Grade III motor block till return of Grade 0.
7. Duration of analgesia i.e. time from onset of sensory block till rescue analgesia.

Assessment of pain was done by Visual Analogue Scale described by Pilowsky I and Bond MR[3] ranges from 0 to 100.

0 – no pain
1-25 –mild pain
26-50 – moderate
51-75 – severe pain
76-100 – very severe

Sedation score based on Ramsey Sedation Score. Side effects and complications were observed. Observations recorded in all these groups were tabulated and statistical analysis carried out by using analysis of variance test (ANOVA) and student 't' test and p value <0.05 was taken as statistically significant and p value <0.001 was highly significant.

RESULTS

Table 1: Demographic data.

Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)
Age (yrs) (mean±SD)	44±10.08	46±10.18	42±11.64
Weight(kg) (mean±SD)	56.1±6.31	58.6±7.09	56.2±5.24
Height (cm) (mean±SD)	158±8.56	160±7.32	161±5.98
Sex (M : F)	11:19	12:18	13:17
Duration of surgery (min) (mean±SD)	88.33±19.53	88.83±14.72	90.17±24.01

The differences were not statistically significant (p<0.05) between the groups.

Table 2: Block characteristics.

Varible	Group I	Group II	Group III	I vs II	I vs III	II vs III
Onset of sensory block (min)	17.73±2.09	9.53±1.59	10.2±1.63	0.000(S)	0.000(S)	0.112 (NS)
Time to achieve highest block(min)	21.48±2.1	12.3±1.5	12.86±1.71	0.000(S)	0.000(S)	0.182(NS)
Two segment regression (min)	157±12.58	212±9.63	208±14.13	0.000(S)	0.000(S)	0.205(NS)
Level of sensory block	T5/T6/T7 1/29/0	T5/T6/T7 2/27/1	T5/T6/T7 1/28/1			
Onset of motor block(min)	19.68±1.72	18.92±2.51	19.98±1.84	0.15(NS)	0.80(NS)	0.272(NS)
Duration of motor block(min)	249±12.28	256±17.86	252±17.79	0.082(NS)	0.453(NS)	0.388(NS)
Duration of analgesia(min)	272±14.72	440±17.86	422.1±20.89	0.000(S)	0.000(S)	0.000(S)

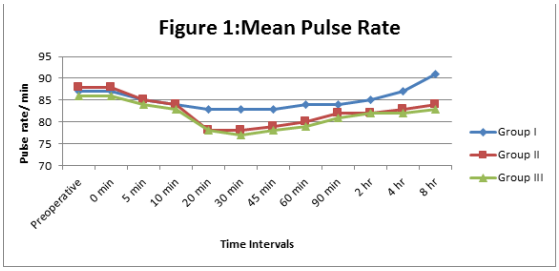
*S - significant*NS – non-significant

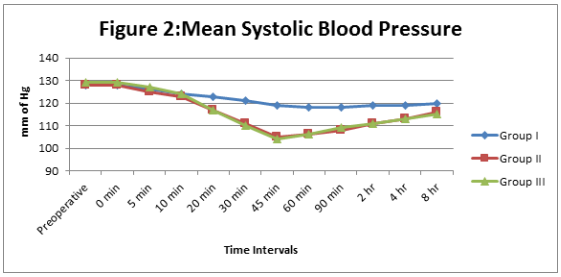
This table shows that there is significant difference between control and study groups for time of onset of sensory block, time taken to achieve highest level of sensory block and two segment regression. Majority of the patients achieved T6 block level. For onset and duration of motor block parameters found to be insignificant between the groups. Duration of analgesia found to be statistically significant between gp I and II, gp I and III as well as gp II and III.

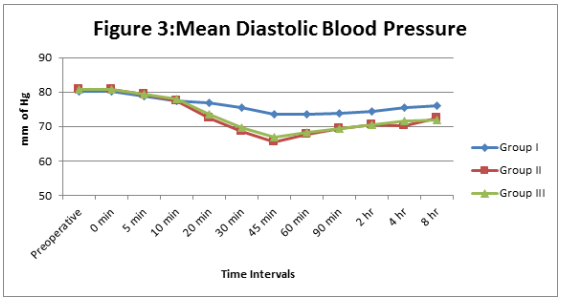
Table 3: Complications.

Variable	Group I	Group II	Group III
Sedation score	0/1/2/3 28/2/0/0	0/1/2/3 27/3/0/0	0/1/2/3 26/4/0/0
Nausea & vomiting	1	1	5
Shivering	2	1	1
Pruritus	0	0	6

Sedation score was found to be 0 in majority of the patients. Pruritis found in 6 patients in gp III i.e. bupivacaine fentanyl group and 5 patients in gp III has post-operative nausea and vomiting.







Graphs show haemodynamic parameters i.e. SBP, DBP found to fall in all groups from baseline and was managed with incremental doses of inj. Mephenteramine and fluid. Pulse rate variations were statistically insignificant between the groups.

DISCUSSION

Exact cellular and molecular effect of clonidine responsible for augmentation of local anesthetic produced sensory block are not completely elucidated. The possible mechanism may be:-

- Clonidine is a lipophilic drug which rapidly and extensively absorbed into spinal compartment after epidural administration and act at spinal nerve root level.
- Suppression of the activity of wide dynamic range neurons and release of substance p in the dorsal horn of spinal cord by activation of pre and post synaptic α2 adrenergic receptors or small primary afferents.
- Release of norepinephrine and acetylcholine in spinal cord dorsal horn.
- Direct inhibition of impulse conduction in A^{δ} and especially C fibres and local anesthetic type of action possibly by increasing potassium conductance.

Onset of sensory block is earlier in gpII and III than in gp I which coincides with study done by Sinatara RS et al[4] reported epidural bupivacaine with fentanyl having the most rapid onset in comparison to bupivacaine –lidocaine or bupivacaine alone. Thomas H et al[5] reported early onset of analgesia with epidural bupivacaine fentanyl than bupivacaine alone. Dobrydnjov I, Samaridtel J[6] reported significant reduction in onset time of spinal block in lidocaine- Clonidine group compared to lidocaine alone. Gabriel et al[7] reported that the addition of clonidine to local anesthetic and opioid mixture reduces the onset time of analgesia of the local anesthetic and opioid mixture.

Exact mechanism of early onset of fentanyl analgesia is not known but may be due to:-

- Fentanyl is lipophilic drug which crosses the dura and enters the CSF.
- Fentanyl increases the nerve conduction of A and C fibres. (Power et al[8])
- Synergistic action between local anesthetic and fentanyl.

Local anesthetic block propagation and generation of neural action potential by a selective effect on sodium channel whereas opioids act on opioid receptors creating an increase in potassium conductance. (Vercanteren M, Meert TF).[9] This action results in hyperpolarisation of the nerve cell membrane and a decrease in excitability (Duggan AW, North RA).[10] Fields et al shows that the primary afferent tissues (dorsal roots) contain opioid binding sites,[11] thus fentanyl might act directly on the spinal nerve or penetrate the dura and act on the spinal roots.

We found epidural bupivacaine fentanyl and bupivacaine clonidine combination increase the duration of two segment regression that corresponds with findings of Gabriel et al[7] and Alves TC[12].

Onset and duration of motor block were found to be statistically insignificant between all the groups. In our study we found epidural fentanyl with bupivacaine did not have any additive-synergestic effect on motor blockade which coincides with study of Peach MJ et al and Lytle HS et al.[13,14] Epidural clonidine also does not have any effect on motor blockade that corresponds with study reported by Le Polainet al,[15] Cook B et al,[16] Kamel HS et al.[17] Present study also coincides with study of Martin et al[18] who reported no difference in motor block in groups having lidocaine alone, lidocaine-clonidine,[18] lidocaine-fentanyl and lidocaine-clonidine-fentanyl groups. Epidural bupivacaine-clonidine had longer duration of analgesia than epidural bupivacaine-fentanyl group and the results corresponds with findings of KizilarshanS et al,[19] Cucchiaro G et al.[20]

Prolonged analgesia in epidural fentanyl group may be due to

- Fentanyl which is a lipophilic drug gets absorbed into the epidural vasculature and epidural pad of fat and slowly gets released and provides prolonged duration.

Prolonged duration of analgesia in epidural clonidine may be due to:-

- Increase acetyl choline concentration in lumbar CSF due to release of acetyl choline in the dorsal horn.
- Clonidine may cause local vasoconstriction thereby reducing vascular removal of local anesthetic surrounding the normal structures.

Post-operative complication i.e. nausea, vomiting are less in epidural clonidine group than epidural fentanyl which coincides with the study of Topcu I et al.[21] Pruritis is more with epidural fentanyl group than epidural clonidine group which coincides with the findings of Sinatra RS et el, Halonen DM et al.[22] In the present study epidural bupivacaine-clonidine group found to be devoid of any marked side effects compared to bupivacaine-fentanyl group which coincides with the studies of Constant I et al [23], Negri PD et al[24], Cucchiaro et al[20].

CONCLUSION

Thus we conclude that clonidine is a safe and better alternative to fentanyl as an adjuvant to epidural bupivacaine hydrochloride for post-operative pain relief because of its prolonged duration of analgesia and fewer side effects.

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